Guidance for Industry

How to Use E-Mail to Submit Information to The Center for Veterinary Medicine

Draft Guidance
For Comment Purposes Only

This draft guidance describes how to use e-mail to submit information to the Center for Veterinary Medicine (CVM or the Center).

This draft guidance represents the Center's current thinking about using e-mail to submit information. It does not create or confer any rights for or on any person and does not bind the Food and Drug Administration (FDA or the Agency) or the public.

E-mail submissions that follow this guidance will be compatible with CVM's current information technology capabilities. This will help ensure the confidentiality, integrity, security, and authenticity of data submitted to the Center. If a regulated sponsor or person wishes to use an electronic approach other than that set forth in this guidance document, the Center will, on request, discuss alternative methods of submitting information.

Comments and suggestions regarding this document should be sent to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fisher's Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the Docket No. 00D-1315.

For questions regarding this draft document, contact Janis R. Messenheimer, Center for Veterinary Medicine, (HFV-135), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-7578, e-mail: jmessenh@cvm.fda.gov.

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Food and Drug Administration
Center for Veterinary Medicine
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IV. PROCESSING PROCEDURES FOR ELECTRONIC SUBMISSIONS

Information transmitted to CVM by e-mail should adhere to minimum standards to ensure confidentiality, integrity, security and authenticity. CVM can process only submissions that comply with the Electronic Records; Electronic Signatures regulation. In addition, procedures described in this draft guidance take into consideration the current information technology capabilities of CVM. Adherence to these standards is verified by the Center's e-mail processing, and generally only submissions in full compliance can be successfully processed as electronic submissions. If sponsors wish to use a different approach, they should discuss it first with CVM.

Sponsors should send each electronic submission as a PDF file (compatible with Adobe® Acrobat® version 4.0) attached to an e-mail. Each e-mail with the attached submission should be sent to cvmdcu@cvm.fda.gov. Submissions are acknowledged with a receipt issued within two working days from CVM's Submission Tracking and Reporting System (STARS) account at stars@cvm.fda.gov confirming the submission was successfully processed.

A. Gateway Information and Communication

The configuration of a sponsor's e-mail software or Internet gateway is critical to the successful interchange of electronic information with CVM over the Internet. Electronic mail formats are not completely standardized, however, most gateways can be configured to accommodate the more recent and reliable formats. Many gateways limit the size of attachments allowed. Therefore, for the purpose of interchange with CVM, the attachment size should be limited to no more than 5 Megabytes (5 MB).

The CVM gateway should have a MIME type e-mail encoding of the level that allows 8-bit or binary attachments for sending e-mail with an attachment.

The sponsor's e-mail software or Internet gateway should be configured to generate "MIME-Version: 1.0" in the header field and recognize the Content-Transfer-Encoding header field in the e-mail message. It should be able to decode all received data encoded by either quoted-printable or Base64 implementation and be able to encode and label 8-bit or binary data using a Content-Transfer-Encoding type of either quoted-printable or Base64 as appropriate. This will allow attached password-encrypted PDF files to be transmitted as part of the transmission package.

The sponsor's e-mail software or Internet gateway should explicitly handle the following media type values:

Text:

- It should recognize and display "text" mail with the character set US-ASCII.
- It should recognize other character sets at least to the extent of being able to inform the user about what character set the message uses.
- It should recognize the ISO-8859 character sets to the extent of being able to display those characters that are common to the ISO-8859 and US-ASCII, namely all characters represented by octet values 1-127.

Multi-part and application:

- It should at a minimum provide facilities to treat any unrecognized subtypes as if they were "application/octet-stream."
- It should offer the ability to remove either of the quoted-printable or Base64 encoding defined in this document if they were used and put the resulting information in a user file.
- It should recognize a mixed subtype and display all relevant information on the message level and the body part header level and then display or offer to display each of the body parts individually.

The following is an example of the items in an Internet e-mail header that CVM uses to identify the sender, the function, or the type of the e-mail.

The table below shows most of the fields in a typical RFC822 header.

Field	Example
From:	Sponsorcontact@sponsor.com
To:	Cvmdcu@cvm.fda.gov
Cc:	Sponsorcoordinator@sponsor.com
Subject:	Email Configuration
Date:	11 May 1998 16:11:43 -0400
Importance:	Normal
Mime-Version:	1.0
Content-Type:	Multipart/mixed; boundary="_NextPart_11:05:1998_(27624)"
Content-Transfer-Encoding:	7bit

When a multipart MIME message is assembled, the text will have a set of lines such as this in front of it, including the part boundary string that was specified in the header.

The example immediately below uses the ISO-8859-1 character set rather than US-ASCII, but limits the characters to 7-bit, that is octets ranging from 1-127:

```
__NextPart__11:05:1998_(27624)
Content-Type: text/plain; charset=iso-8859-1
Content-Transfer-Encoding: 7bit
```

The lines in the example below might precede an attached file called cvmform.pdf:

```
__NextPart__11:05:1998_(27624)
Content-Type: application/octet-stream; name=cvmform.pdf
Content-Transfer-Encoding: base64
```

Note that the content is identified simply as "application/octet-stream". If PDF had been defined to the originating e-mail agent, it might have been identified as "application/pdf". If PDF was defined to the receiving agent as a type that should be processed by Adobe® Acrobat®, the agent would launch Acrobat® to view the file. When the receiving agent does not recognize the Content-Type, it should treat it as "application/octet-stream," decode it, and offer the recipient the option to save it as a user file.

B.   E-mail Address

Senders should register their e-mail addresses with CVM as outlined in Section III. This will allow CVM to process the sponsors' submissions. The e-mail address registered with CVM should match exactly the e-mail address of the received submission.

C.   Subject Line of E-mail

The subject line is an integral part of CVM's processing of electronic information submitted by e-mail. Each electronic submission of information is identified, checked, and processed based on the subject line of the e-mail message. The subject line for an e-mail message containing an attached submission should be the single word identified in the appropriate guidance. It should be only the single word, capitalized, non-quoted, and should contain no special characters. Any additional information in the subject line will cause a fatal error and CVM will not be able to process the submission.

The following are subject lines which should be used for electronic submission to CVM.

Subject Line	Type of Electronic Submission
REGISTER	Electronic copy of registration letter specifying sponsor's intent to submit information electronically
CHANGE	Electronic notification of changes in conditions of registration
PASSWORD	Electronic request to change an individual password

D.   PDF File of Electronic Submission

For purposes of any electronic submission, the sponsor should use the appropriate format provided by CVM, which should be submitted to CVM as an encrypted PDF file (compatible with Adobe® Acrobat® version 4.0) attached to an e-mail message. Forms for electronic submissions are available on CVM's Home Page, http://www.fda.gov/cvm. The sponsor should create a word processing document with the necessary data and convert it to a PDF file, or fill in a PDF form directly.

There should be only one PDF attachment per e-mail, and it should be no larger than 5 Megabytes (5 MB) in size. It should conform to the format and standards for the specific type of electronic submission as detailed in the guidance. The Center's automated processing performs a check of the number of attachments and will not process an electronic submission with more than one attachment.

Sponsors should use ISO 9660 Interchange Level 1 file naming convention, i.e., up to 8 characters (A-Z, 0-9, and _) for the file name and PDF for the file extension (8.3 naming convention); an example using this convention would be filename.PDF.

E.   Electronic Signature

Each individual who intends to submit electronic submissions will have a unique electronic signature to verify the sender's identity. The unique electronic signature will consist of the sender's e-mail address and the individual password.

This individual password should consist of 12 case-sensitive alphanumeric characters. The sender uses the individual password to encrypt the file before transmitting it to CVM. Only CVM's electronic submission system and the person who submits the electronic submission should know the individual password and be able to open the file.

CVM will acknowledge receipt of the electronic submission by creating a new e-mail message (i.e., not by using a "Reply" feature) and sending it to the e-mail address of the individual submitting the electronic submission. The receipt will be a password-encrypted file of routing information from STARS attached to an e-mail message. CVM will use the sponsor password to encrypt the file.

Individuals who submit information electronically must follow the electronic signature requirements described in 21 CFR 11.100-11.300. These requirements must be followed for CVM to accept electronic submissions as the official copy, instead of paper. If sponsors are not capable of meeting these requirements sponsors must submit information on paper. With regard to the procedures set out in the draft guidance that the sponsors should use to submit information electronically, on request CVM will discuss alternative methods of submitting the information.

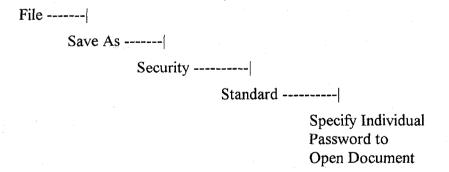# V. SECURITY MEASURES FOR ELECTRONIC SUBMISSIONS

Corporations have used the Internet as an expeditious vehicle for the exchange of information for several years. However, many corporations and government agencies have avoided using the Internet for the exchange of sensitive and/or confidential information because of concerns about security. In developing an electronic submission project using the Internet as the message-carrying vehicle, four areas of security should be addressed adequately by all participants prior to its adoption.

A. Disclosure/Non-Disclosure

Information submitted to CVM is subject to the Freedom of Information Act and FDA's regulations on public information at 21 CFR Parts 20 and 514. Some information, such as trade secrets, certain commercial and financial information is confidential in nature and is nondisclosable. Therefore, using the Internet to submit confidential information can be done only with adequate encryption. CVM currently recommends that this encryption be in the form of a password-protected PDF file. CVM will continue to monitor and assess the adequacy of this level of security and determine whether or not a different encryption method is necessary.

Protecting the Confidentiality of the Information in Electronic Submissions

When the PDF file is created, the person submitting the electronic information will encrypt the file with his/her individual password. In Adobe®Acrobat®, this is done by selecting:

File -------|

        Save As -------|

                Security ----------|

                        Standard ----------|

                                Specify Individual
Password to
Open Document

Authentication Verification

Currently, CVM receives paper submissions from sponsors by US Postal Service, Federal Express, United Parcel Service, etc. With these submissions, there is a cover letter on sponsor letterhead signed by an authorized sponsor official. This information allows CVM to authenticate that the submission is from the stated sponsor. Any electronic submission should also provide a

means by which CVM can authenticate the origin of the electronic document, such as the unique two-part electronic signature.

Unique Two-Part Electronic Signature

The registration letter should contain the name and e-mail address for each authorized sender. Subsequent to the receipt of CVM's acknowledgment letter, each sender should submit to CVM an individual password as described in Section III.B of this guidance. The unique combination of the e-mail address and the individual password will serve as the electronic signature under 21 CFR 11.200(a)(1) and will authenticate the identity of the sender. CVM will maintain a database of electronic signatures and will automatically reject any electronic submission received that does not match the unique combination of e-mail address and individual password.

Verification of the Sender's Identity

An additional precaution will be taken to ensure that the e-mail message received at CVM did indeed come from the sender designated. CVM will acknowledge receipt of the electronic submission by creating a new e-mail message (i.e., not by using a "Reply" feature) and sending it to the e-mail address of the sender. This e-mail message will have a PDF attachment encrypted with the individual password. If a sender receives an acknowledgment but has not sent an e-mail to CVM, he/she should immediately report this to CVM by telephone to 301-827-8277.

B.   **Verification of Date of Submission**

Currently, time-sensitive information is submitted by certified mail so that the sponsor has a record verifying the date and name of an individual who received the information at CVM. This also provides a legal basis by which drug sponsors can assert their compliance with laws and regulations.

Currently, CVM uses the date on the cover letter to determine whether information was submitted within the time required by statute or regulation. The sponsor should include a date within the PDF electronic submission file. If CVM is able to open and read the file, the date within the file will serve as the date of submission.

CVM's Acknowledgment of Electronic Submissions

The acknowledgment of receipt will be an e-mail message with an attached encrypted PDF file containing information from CVM's tracking system. CVM will use the sponsor password to encrypt this file before sending the acknowledgment to the sender.

If the sender has not received an acknowledgment by the third working day after sending in the electronic submission, they should call CVM at 301-827-8277.

C.   Submission Integrity

The integrity of the content of a submission to CVM is the responsibility of the sponsor. If sections of a paper submission are missing or illegible, CVM requires the sponsor to provide copies of the missing or illegible information. A remote possibility exists that intentional or unintentional changes could be made to an electronic submission that could not be made to a paper submission. For example, unintentional "scrambling" of the submission may occur during transmission so that CVM receives a corrupted, unusable file. Further, a submission could be intentionally changed if a message is intercepted en route, changes are made to the content and then the message is sent on as if from the original sender.

CVM will rely on the password encryption of the PDF file to ensure the integrity of the electronic submission. If the file is received by CVM intact and can be decrypted and opened by Adobe® Acrobat®, then CVM will assume no changes occurred to the submission once it was e-mailed from the sponsor. If CVM receives a corrupted file and can identify who the sender is, CVM will notify the sender that its file was corrupted and the sender should resubmit the file.

VI. CHECKLIST FOR ELECTRONIC SUBMISSIONS

To make electronic submissions, sponsors should:

- Have MIME (base64) compliant access to the Internet. See Section IV.A for details.
- Use the appropriate form or format provided by CVM.
- Conform to an ISO 9660 Interchange Level 1 compatible naming convention for PDF files e-mailed to CVM. The name of the attached file should be 8 characters or less with the letters PDF as an extension, i.e., xxxxxxxx.PDF. See Section IV.D for details.
- Register with CVM once for all types of submissions listed in the Electronic Submission Docket.

REGISTRATION PROCESS (See Section III for details.):

1. Send a single, original, signed registration letter to CVM. See Section III.A. for an example of the registration letter. The letter should contain:
   a) name, mailing address, phone number, and e-mail address of the Sponsor Coordinator;
   b) names, mailing addresses, phone numbers, and e-mail addresses for each person who will submit electronic submissions;
   c) a 12 character, case-sensitive alphanumeric character sponsor password. See Section III.A for details;
   d) the subject of letter should be **Registration Letter for Electronic Submission to CVM** to clearly identify the purpose of the letter.

2. Create a PDF copy of the registration letter. Encrypt the PDF file with the sponsor password, attach it to an e-mail message, and send it to cvmdcu@cvm.fda.gov. The subject line of the e-mail message should be the word **REGISTER**.

3. CVM will send an e-mail to the Sponsor Coordinator named in the registration letter. The message will have an encrypted PDF file attached containing an acknowledgment of receipt of the registration letter. The password necessary to decrypt the PDF file receipt will be the sponsor password sent in the registration letter. A paper response will also be sent. If the sponsor has not received both of these acknowledgments within three working days contact CVM by calling the electronic Document Control Unit at 301-827-8277.

4. The Sponsor Coordinator and each identified contact should choose an individual password before sending an electronic submission. Directions for informing CVM of the new individual password will be included in the Center's response to the registration letter. The subject line of the e-mail message should be **PASSWORD**. See Section III.B of this guidance for details.

5. The sponsor should not send an electronic submission until CVM acknowledges the receipt of an individual password by e-mail.